

REMARKS

Reconsideration of the Examiner's rejection of the present application is requested respectfully in view of the above amendments and the following remarks.

STATUS OF THE CLAIMS

Claims 1-20 and 25-29 were pending at the time of the present Office Action. Claims 25, 26 and 29 stand withdrawn from consideration. Claim 15 has been amended. Claim 20 has been canceled. No new matter has been added by these amendments. Therefore, claims 1-19 and 27-28 are now presented for review.

SUMMARY OF OFFICE ACTION

An objection has been made to the claim to Priority under 35 U.S.C. 119 (a)-(d) based on an application filed in France on June 14, 1996. As discussed below, the records of the USPTO verify that this priority claim is correct.

An objection has been made regarding the amendments to claims 15 and 20 made in the previous response filed June 13, 2008, because the amended claims did not show the text added and deleted. The amendment to claim 15 has been resubmitted in the present response. Claim 20 has been canceled. In the previous response, clean copies of the amended claims were inadvertently submitted instead of the marked-up copies.

An objection has been made regarding the clarity of the chemical figures in claims 2, 10-12, and 15.

Claims 2, 10-12, and 15 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite because the chemical figures are considered to not legible.

Claims 1-19, 27 and 28 stand rejected under 35 U.S.C. §103(a) as being unpatentable over the combined teachings of Petitou et al. (US 5378829) in view of Oosta et al. (of record).

Claim 20 stands rejected under 35 U.S.C. §103(a) as being unpatentable over the combined teachings of Petitou et al. (US 5378829) in view of Oosta et al. (of record), further in view of Paoletti et al. (of record). This claim has been canceled, rendering this rejection moot.

OBJECTION REGARDING PRIORITY

In the present Action, the Examiner has noted that the earliest US application in the priority chain is US 09/202241 filed December 10, 1998, and that that application claims priority to a French application filed June 14, 1996, more than 12 months earlier. It is believed that this objection is based on the Filing Receipt of the present application which appear to be in error.

The image file wrapper of US 09/202241 is not available on the PAIR system because of its age. Therefore, attached to this response is a copy of the Filing Receipt which applicants received for the US 09/202241 application. This Receipt clearly shows that US 09/202241 was a Section 371 filing of PCT/FR97/01048 filed June 11, 1997, which is within one year of the priority French Application No. 96 07457, filed June 14, 1996. December 10, 1998 was the Section 371 US filing date.

As further confirmation, a copy of the first page of the Filing Receipt of US 09/686373, the parent of the present application is also attached. This Receipt also shows the Section 371 filing status of the earlier US 09/202241 application.

In addition, a claim for priority to PCT/FR97/01048 is included in the original Declaration which is a part of the record of the present application.

For all of these reasons, the Examiner is respectfully requested to withdraw the present objection and confirm the propriety of the claim of priority to French Application No. 96 07457, filed June 14, 1996.

A separate Request for Corrected Filing Receipt will also be filed by Applicant.

OBJECTION REGARDING CLAIMS 15 AND 20

As noted above, the amendments to claim 15 submitted in the previous Response is resubmitted herein in proper format. Claim 20 has been canceled. This should overcome this objection.

OBJECTION AND REJECTION UNDER 35 U.S.C. §112 OF CLAIMS 2, 10-12, and 15

An objection has been made regarding the clarity of the chemical figures in claims 2, 10-12, and 15. Furthermore, claims 2, 10-12, and 15 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite because the chemical figures are considered to not legible.

These claims have been amended to include clearer chemical figures. It is submitted that the claims as amended are now clear, and that the present objection and rejection have been overcome.

CLAIM REJECTION UNDER 35 U.S.C. §103(a)

Claims 1-19, 27 and 28 stand rejected under 35 U.S.C. §103(a) as being unpatentable over the combined teachings of Petitou et al. (US 5378829) in view of Oosta et al. (of record). Applicants respectfully traverse this rejection.

As discussed in the previous response, the claims of the present application are directed to synthetic polysaccharides containing 8 to 24 monosaccharide units, further characterized as set forth therein. As explained in the specification, at page 2, lines 4-9, prior to the present invention short chain oligosaccharides were known, such as those described in US 5,378,829, which the Petitou reference cited as the primary reference in the present rejection. citation. But as discussed previously, and as noted by the Examiner, Petitou only describes oligosaccharides having a maximum of 7 monosaccharide units. The Examiner has not cited any other references that teach synthetic polysaccharides of more than 7 units, and Petitou is clearly limited to this size.

Oosta is cited by the Examiner as a secondary reference to show that various larger size polysaccharides were known in the art, and that larger heparin fragments exhibit greater biological activities than hexasaccharides. The Examiner then indicates that the teachings of Oosta would have motivated one skilled in the art to use the Petitou technique to produce polysaccharides of more than 7 units. Applicants respectfully disagree with this conclusion.

Oosta is a 1980 reference which describes a method of fractionating heparin. As known in the art, the starting material heparin is itself a heterogeneous product, composed of a great number of oligosaccharidic chains differing in their chemical structure as well in their length. According to Oosta, the oligosaccharidic chains naturally occurring in heparin substances are fractionated into mixtures of various length fragments, which are then separated by use of a chromatographic column. At the time of Oosta, such oligosaccharides were made by fractionating natural heparins (particularly pig heparin) rather than by stepwise synthesis. That is, Oosta discusses the biological activities of oligosaccharide fractions isolated from a mixture resulting from chemical depolymerization of heparin (see the first paragraph of the Discussion section on page 832: "We have randomly cleaved preparations of heparin ... by using appropriate chemical techniques."), and subsequent separation of fractions with different sizes by

gel filtration and affinity fractionation. Products obtained by such techniques are different from the claimed oligosaccharides, and different from the oligosaccharides synthesized by Petitou. The oligosaccharides of the present invention and those of Petitou are obtained by stepwise synthesis of specific building blocks intermediates. In the present claims and in the claims of Petitou, all of the R side groups, attached though an O linkage to the saccharide chain, are limited to either alkyl or SO_3^- groups. This allows for the synthesis of unique products by the intentional selection of the side groups and their locations on the saccharide chain. On the other hand, the natural heparin derived fractions obtained by Oosta are heterogeneous products, comprising mixtures of different oligosaccharides having the same length (but varying in their monosaccharidic constituents) as well as the residual presence of shorter or longer chains. The larger the fraction, the higher the heterogeneity of the fraction. For example, in Table 1 of Oosta the fractions of 14 or 16 residues are prefaced by the approximation symbol "~". Even in the lowest fraction (hexasaccharide), hundreds of different compounds may be found, since different sugars may be present and different substitution patterns thereof may occur. The teachings of Oosta, therefore, would not enable one to conclude that an individual component within a given fraction would necessarily have improved biological properties compared to another individual component taken from a fraction with lower length. The teachings of Oosta are limited to fractions comprising mixtures of hundreds of components.

As described in Oosta, (which was published over 25 years ago) the functional saccharide fragments discussed therein were all made by random scissioning of long-chain porcine heparin. These random length fragments were then examined for their properties. Not only is there no description, or even a suggestion, that these fragments could be synthesized, but there is not even any teaching of how to accurately extract a particular fragment. There is also no discussion of what monomeric saccharide groups are present, or what side groups are on those saccharides. Since the scissioning was random, the chemistry and properties of the fragments was also random. This may have been useful early research in development of fractionated heparin compositions, but in no way provides any teaching that longer chain fragments, or any fragments for that matter, could be specifically synthesized. As noted above, the saccharides of Petitou and those of the present invention are specifically made to provide a known substrate with known side groups.

At the time the Petitou reference was published, references such as Oosta describing fractions from natural heparins were well known. Several of these are also cited at page 2 of the

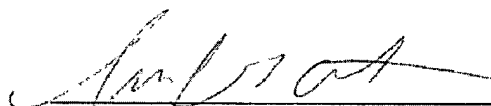
present specification. However, Petitou did not look to lengthen his oligosaccharide chains to more than seven units. Instead, Petitou looked to obtain improved properties by selectively substituting different R side groups at different specific locations on the underlying saccharide chains. This is amply shown by the various compounds set forth in the examples of Petitou. Although longer saccharide chains derived from natural heparin fractions were well known in the art, Petitou was not motivated to even attempt to synthesize longer chains compounds. It is only with hindsight derived from the teachings of the present inventors that one would be motivated to synthesize oligosaccharide chains of 8 to 24 units as claimed herein. For these reasons, the Examiner is respectfully requested to reconsider and withdraw the present rejection of claims 1-19, 27 and 28 under 35 U.S.C. §103(a) over this combination of references.

Claims 20 also stands rejected under 35 U.S.C. §103(a). However, this claim has been canceled, rendering this rejection moot.

It is submitted that the claims in the present application are now in condition for allowance, and action to that effect is respectfully requested.

The Commissioner is hereby authorized to charge any additional fees or credit any overpayment resulting from this Amendment to Deposit Account 18-1982.

Respectfully submitted,



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